REMARKS/ARGUMENTS

Claims 1, 8-12, 19-25, and 32-35 are active in this application. Claim 1 is drawn to the elected subject matter. Support for the amendment to Claim 1 is found in Claim 6. No new matter is added by these amendments. Applicants request rejoinder of claims 12, 22-25 and 32-35 upon finding that Claim 1 is allowable (MPEP 821.04).

As amended herein, the present claims are to a modified enzyme comprising the amino acid sequence of SEQ ID NO:2 and which has increased NAD(H) affinity compared to the wildtype enzyme. Hummel et al.

The rejections of Claim 1 under 35 U.S.C. § 102(b) or 102(e) are obviated by amendment.

The rejection of Claim 6 under 35 U.S.C. § 103(a) over Hummel et al. is obviated by the cancellation of Claim 6. As this rejection may apply to amended Claim 1, the rejection is respectfully traversed.

Hummel et al. does not describe a modified enzyme comprising the amino acid sequence of SEQ ID NO:2. Hummel et al. describes reducing the basic nature of the coenzyme-docking site by exchanging positively charged for uncharged amino acids and/or by replacing neutral or positively charged amino acids with negatively charged amino acids (see column 1, lines 54-61). Notwithstanding this deficiency, the Office has taken the position that it would have been obvious to select any one of the four mutations in the alcohol dehydrogenase and particularly the G38D mutation with a reasonable expectation of success. Applicants disagree Hummel et al specifically describe making at least three or four mutations in the enzyme and as a result one reading the Hummel et al disclosure would understand to make an improved alcohol dehydrogenase one would have to use those combinations of mutations. For this reason alone, Claim 1 is not obvious in view of Hummel et al.

In any case, Applicants have already described in detail how the claimed enzyme is vastly better in a number of indicia relative to an enzyme from Hummel et al. For the sake of convenience a discussion of those differences are again reiterated below.

As described in the specification on page 3, lines 14-19, referring to the work described in Hummel et al. (with reference to the PCT equivalent WO 99/47684):

> Other mutants in which an additional replacement of a neutral amino acid by an acidic amino acid (G38D) was performed along with the above-mentioned replacements of basic amino acids by neutral amino acids (replacements R39L, K48M as well as the charge neutral replacement A9G), indeed exhibited broadening of the coenzyme affinity towards NAD(H), but was also considerably unstable and obtainable only with low yields.

This statement is supported by the data presented in the Table on page 22 of the present application. In particular, Applicants direct the Examiner's attention to column 3: "Mutant 2" rows 5 and 6 where the thermal stability was measured (also refer to page 21, lines 3-4 noting that Mutant 2 is per WO99/47684, i.e., Hummel et al.).

The data presented in this table also demonstrates that the claimed G38D modified enzyme had significantly higher thermal stability at both 30°C and 42°C relative to the Hummel et al mutant. In addition, the claimed G38D modified enzyme had improved NAD affinity relative to wildtype (referring to the data and supporting discussion in the paragraph bridging pages 22 and 23).

There is nothing in the Hummel et al disclosure which would have suggested that making only a G38D mutation in the alcohol dehydrogenase enzyme would possess such superior properties compared to those enzymes described in Hummel et al. Accordingly, Applicants request that this ground of rejection be withdrawn.

The rejection of Claim 1 under 35 U.S.C. § 112, second paragraph is obviated by amendment.

Finally, Applicants request that allowance of this application.

Respectfully submitted,

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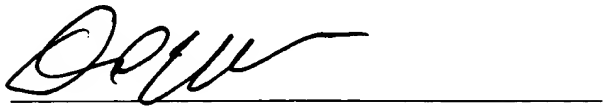
MAIER & NEUSTADT, P.C.



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